

INTRODUCTION

Although previous epidemiological studies have reported a bidirectional association between depressive symptoms and cognitive impairment, the long-term dynamic interaction between these two factors specifically during midlife-a critical period when most modifiable dementia risk factors converge-remains unexplained. This study aimed to examine the long-term interaction between depressive symptoms and cognitive function over a 13-year period, and explore the underlying neuroimaging mechanism in multi-regional middle-aged individuals.

METHODS

Paticipants:

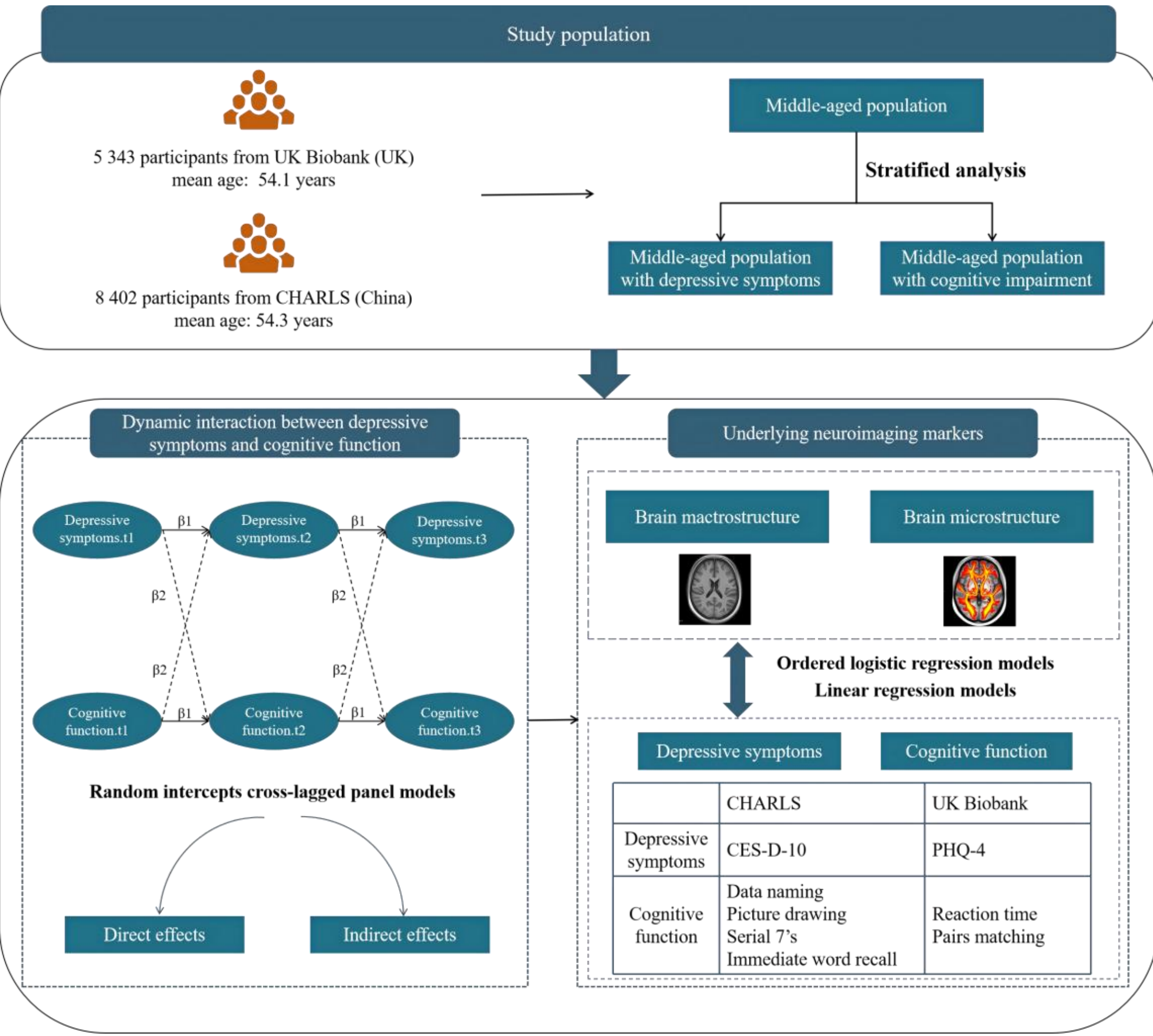
Three waves of data from the CHARLS and UK Biobank, with participants aged 4065.

Long-term interaction analysis:

Random intercepts cross-lagged panel model to analyze long-term interplay of depressive symptoms and cognitive function.

Underlying neuroimaging measures:

Ordered logistic and linear regression models in the UK Biobank to examine the associations of depressive symptoms or cognitive function with brain measures.



RESULTS

Participant characteristics

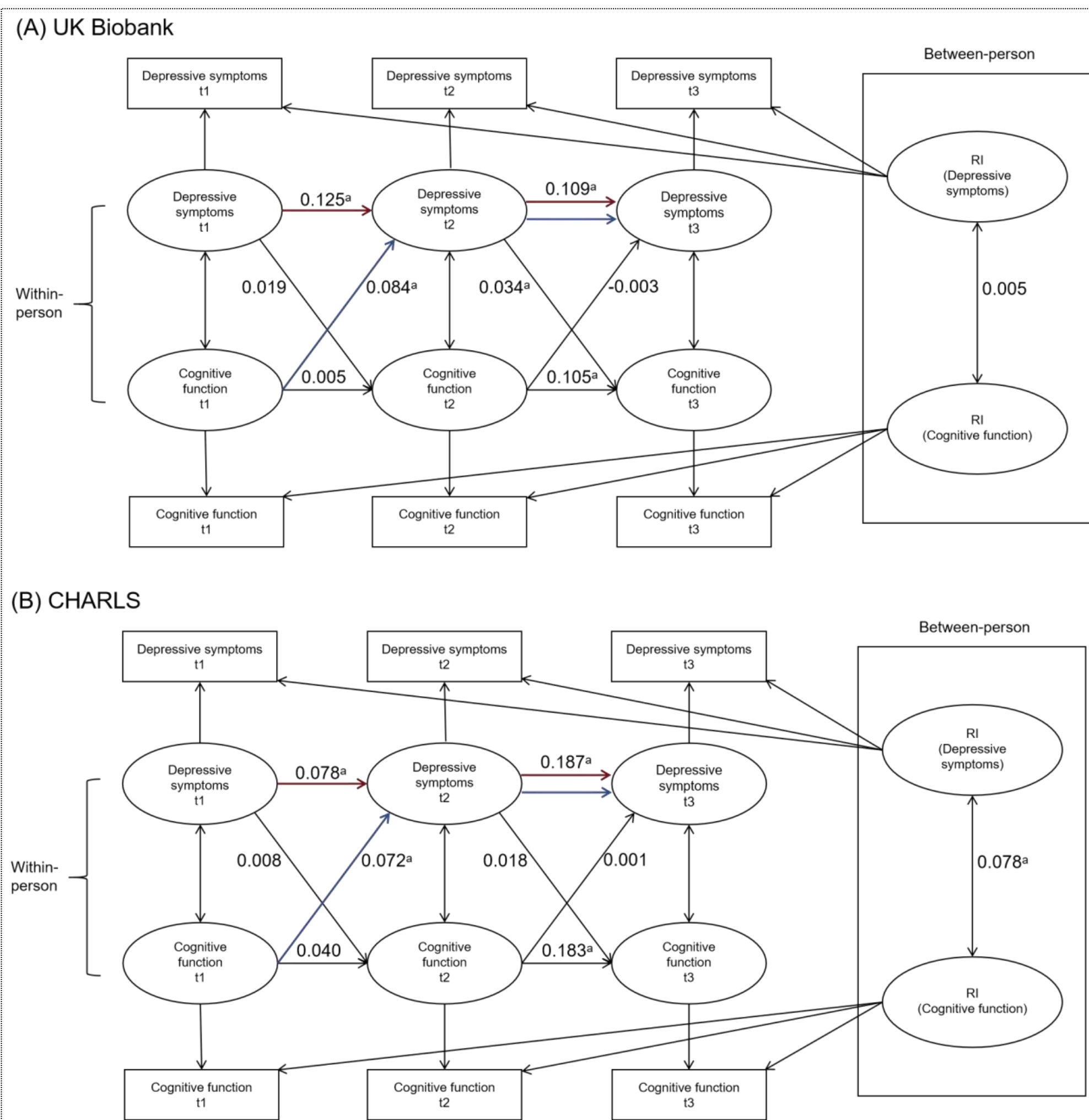
	
8402 participants	5343 participants
54.1 ± 6.6 years	54.3 ± 5.9 years

Long-term dynamic interactions

- Poorer baseline cognitive function was associated with more severe and persistent depressive symptoms subsequently (UK Biobank, $\beta=0.009$, 95%CI 0.001 to 0.021; CHARLS, $\beta=0.013$, 95%CI 0.005 to 0.023).
- Among participants with depressive symptoms at baseline, poorer cognitive performance was associated with subsequent greater depressive symptoms, which in turn led to subsequent poorer cognitive function (UK Biobank, $\beta=0.025$, 95%CI 0.001 to 0.073; CHARLS, $\beta=0.006$, 95%CI 0.001 to 0.015).

Neuroimaging correlations

- Participants with greater depressive symptoms exhibited significantly larger white matter hyperintensity volume and larger mean diffusivity value (UK Biobank, $\beta=0.101$, 95%CI 0.021 to 0.178; CHARLS, $\beta=0.097$, 95%CI 0.015 to 0.178).



Characteristic	Standardized coefficient (95% CI)	P value
GMV	-0.013 (-0.104 to 0.077)	0.776
WMV	0.054 (-0.021 to 0.130)	0.160
WMH	0.101 (0.021 to 0.178)	0.011
FA	-0.055 (-0.135 to 0.026)	0.179
MD	0.097 (0.015 to 0.178)	0.020

Abbreviations: GMV, volumes of total gray matter; WMV, volumes of white matter; WMH, volumes of white matter hyperintensity; FA, fractional anisotropy; MD, mean diffusivity.

DISCUSSION

In this three-wave cohort study of middle-aged adults across 2 countries, poorer cognitive performance was associated with sustained greater depressive disorders later. These findings highlighted the potential of improving cognitive performance to reduce later depressive disorders.

Correspondence

Yaping Zhang, School of Public Health, the Second Affiliated Hospital of School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China.
Email address: yapzhang@zju.edu.cn

¹School of Public Health, the Second Affiliated Hospital of School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China

²Nanhu Brain-computer Interface Institute, Hangzhou, Zhejiang, China

³Department of Nursing, the Second Affiliated Hospital of School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China

⁴Department of Psychiatry, the Second Affiliated Hospital of School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China

⁵Key Laboratory of Intelligent Preventive Medicine of Zhejiang Province, Hangzhou, Zhejiang, China